REMARKS

This is in response to the Final Official Action for the above-captioned application mailed April 1, 2004. New Claims 23-34 have been added. Claims 1 – 34 are pending in the application. Claims 1, 8, 9, 10, 14 and 20 have been amended as described herein. No new matter has been introduced by virtue of the amendments made herein, as will be clear from the description of the amendments hereinbelow. Applicants respectfully request reconsideration and withdrawal of the rejection set forth in the January 29, 2003 office action, and solicit the issuance of a notice of allowance. If a telephone interview is deemed to be helpful to expedite the prosecution of the subject application, the Examiner is invited to contact applicant's undersigned attorney at the telephone number provided.

Claims 1-7 and 9-22 have been rejected under 35 USC 112, second paragraph as allegedly indefinite. For the sake of expediting prosecution, Applicants have cancelled recitations beginning with "especially," "such as" and "including" from Claims 1, 9 and 10, as well as the specific serotonin reuptake inhibitors and tricyclic antidepressants of Claims 14 and 20. New Claims 23-27, 28-32, 33, and 34 have been added to recite the limitations cancelled from, respectively, Claims 9, 10, 14 and 20 identified above. It is respectfully submitted that new Claims 23-34 do not introduce new matter.

In view of the foregoing, withdrawal of the rejection of Claims 1-7 and 9-22 under 35 USC 112, second paragraph as allegedly indefinite is respectfully requested.

Claims 9 and 10 have been rejected under 35 USC 112, first paragraph as allegedly non-enabled by the specification. The Official Action relies on the *Ex parte Forman* or *In re Wands* factors to conclude that a person with skilled in the art would have to carry out undue experimentation in order to practice the claimed invention.

However, it is respectfully submitted that Claims 9 and 10 are enabled by the specification. Purely for the sake of expediting prosecution, Claims 9 and 10 have been amended to delete the recitations of inflammatory disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; ulcer; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; head trauma; spinal cord trauma; ischemic neuronal damage, including cerebral ischemia, for example cerebral hippocampal ischemia; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, including bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human-animal interaction stress in dogs; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; osteoporosis; and premature birth in a mammal or bird. Claims 9 and 10 are enabled by the specification, as shown by the analysis of the *In re Wands* factors is given below.

With regard to factor 1, the claims as amended are narrow in scope. The above-identified conditions that have been cancelled from Claims 9 and 10 include conditions specifically identified by the Official Action (See, e.g., page 5, section titled "The breadth of the claims"). The remaining conditions recited in the claims would be understood by one skilled in the art to be sufficiently related that an enabling teaching of the treatment of one condition would enable one of skill in the art to treat another of the remaining conditions. Thus, since, as acknowledged by the Examiner, the disclosure is enabling for the treatment of, for example, depression (see, page 4, para. 2, first sentence), which is included in the recitation of Claims 9 and 10, and was included in Claims 9 and 10 as originally filed, it is respectfully submitted that Claim 9-10 as amended are enabled by the disclosure.

With regard to factor 2, it is respectfully submitted that the guidance in the instant specification is sufficient to support Claims 9-10. In particular, the instant specification discloses in sufficient detail doses for the CRF antagonists needed for the treatment of the claimed conditions. As previously noted, the Official Action acknowledged that the treatment of depression is enabled by such a disclosure. It is respectfully submitted, accordingly, that the treatment of the remaining conditions recited in the claims as amended, which are sufficiently related as noted hereinabove, is also enabled.

With regard to factor 3, each of the conditions referred to by the Official Action has been cancelled from the claims as amended. Accordingly, the state of the prior art does not affect the enablement of Claims 9-10 as amended.

With regard to factor 4, although not addressed expressly by the Official Action, it is respectfully submitted that the level of the person of ordinary skill in the art is high. The person of ordinary skill is often a scientist with an advanced degree in the field and with several years of industrial experience. Accordingly, the teaching required is less than would be required for most inventions in other arts.

With regard to factor 6, the specification provides detailed disclosure of dosages for the active compounds recited in the claims. No more than routine experimentation, if any at all, would be required to treat a patient based on the teachings of the instant specification. There would therefore be no "undue" experimentation, as would be required to find the specification non-enabling.

At most, the Official Action could attempt to rely on the unpredictability of the art (factor 5). However, even assuming that this factor weighs in favor of unpredictability of the instant claims, the balance of the *In re Watts* factors clearly weighs in favor of a finding that the instant claims are enabled by the specification.

In view of the foregoing, withdrawal of the rejection of Claims 9 and 10 under 35 USC 112, first paragraph as allegedly indefinite is respectfully requested.

Claims 12-16 and 18-22 have been rejected under 35 USC 112, first paragraph as allegedly non-enabled by the specification. The Official Action states that "many of the second thrapeutic agents can have adverse drug interactions" (Official Action, page 7, lines 12-13), and

concludes that a person with skilled in the art would have to carry out undue experimentation in order to practice the claimed invention.

However, it is respectfully submitted that Claims 12-16 and 18-22 are enabled by the specification. Applicants note, as a preliminary matter, that the Official Action has not applied the *In re Wands* factors to Claims 12-16 and 18-22. An analysis of the *In re Wands* factors shows that the claims are enabled. In particular, with regard to factor 1, Claims 12-16 are narrow in scope, as they are directed to only a few, very well-defined conditions; with regard to factor 2, the instant specification discloses in sufficient detail doses for the CRF antagonists needed for the treatment of the claimed conditions, whether alone or in combination; with regard to factor 4, the level of the person of ordinary skill in the art is high; with regard to factor 6, the specification provides detailed disclosure of dosages, as noted above, so that no more than routine experimentation, if any at all, would be required to practice the invention claimed in Claims 12-16 and 18-22. There would therefore be no "undue" experimentation, as would be required to find the specification non-enabling.

At most, the Official Action could attempt to rely on the unpredictability of the art (factor 5). or the state of the art (factor 3). However, even assuming that these factors weigh in favor of unpredictability of the instant claims, the balance of the *In re Watts* factors clearly weighs in favor of a finding that the instant claims are enabled by the specification. Moreover, the Official Action merely alleges that "adverse drug interactions" could occur, and that one of the recited agents "interferes with the metabolism of other drugs" (Official Action, page 7, lines 12-14), but provides no evidence to support its statements with regard to adverse interactions with, or interference with the metabolism of, the particular drugs at issue, *i.e.,* the compounds of claim 1. Furthermore, Applicants respectfully point out that, in order to counter the Official Action's allegations regarding adverse drug interactions and inteference with the metabolism of other drugs, Applicants would be obligated to provide *in vivo* data. It is well established, however, evidence of *in vivo* activity is <u>not</u> required for patentability. For example, an Applicant does not have to provide "that a correlation exists between a particular activity and an asserted therapeutic use of a compound..." MPEP 2107.03, section I. In addition, "in no case has a Federal Court required an applicant to support an asserted utility with data from human clinical trials." MPEP 2107.03, section III. Moreover, "absolute certainty [of the operability of an invention] is not required by law." *Id.* (citing *In re Wooddy,* 331 F.2d 636, 639 (CCPA 1964)). Accordingly, the Official Action inappropriately places on the Applicant a burden of proof that the law does not require.

In view of the foregoing, withdrawal of the rejection of Claims 12-16 and 18-22 under 35 USC 112, first paragraph as allegedly indefinite is respectfully requested.

Claims 1-7, 9 and 10 have been provisionally rejected under the judicially created doctrine of obviousness double patenting as allegedly obvious over Claims 1-9, 13, 14, 29-35 and 37-40 of copending application No. 09/580,791.

Applicants submit herein, without prejudice and in the interest of facilitating prosecution, a terminal disclaimer that overcomes the rejection of Claims 1-7, 9 and 10 under the judicially

created doctrine of obviousness double patenting. Withdrawal of the rejection is respectfully requested.

Claims 1, 3, 5-11 and 17 have been rejected under 35 USC 102 as allegedly anticipated by Chen (WO 95/33750). According to the Examiner, the cited reference is anticipatory for A = CH, $R_3 = CH_3$, B = NR_1R_2, wherein R_1 and R_2 are independently C_2-C_3 alkyl; $R_4 = CONR_{24}R_{25}$ or $COOR_{24}$; Z = O; R_5 = phenyl.

However, it is respectfully submitted that Claims 1, 3, 5-11 and 17 are not anticipated by Chen. Claim 1 has been amended for the sake of expediting prosecution to delete the recitation "C_1-C_6 alkyl" from the definition of R_1. Claims 6 and 7 have been similarly amended. Chen does not disclose R_1 as defined in Claims 1, 6 and 7 as amended. With regard to Claim 8, purely for the sake of expediting prosecution, the compound recited in the last line of Claim 8 of the instant application has been cancelled. Claim 8 has also been rewritten in independent form.

In view of the foregoing, Chen does not anticipate Claims 1, 3, 5-11 and 17. Withdrawal of the rejection under 35 USC 102 of Claims 1, 3, 5-11 and 17 as allegedly anticipated by Chen is respectfully requested.

New Claims 23-27, 28-32, 33, and 34 have been added to recite the limitations cancelled from, respectively, Claims 9, 10, 14 and 20 identified above. It is respectfully submitted that new Claims 23-34 do not introduce new matter. It is respectfully submitted that the new claims, which depend on patentable claims, are themselves patentable. Applicants further point out that new Claims 25 and 26, dependent on Claim 9, and new Claims 30 and 31, dependent on Claim 10, are directed to depression and forms of depression, which are supported by an enabling disclosure, by Examiner's own acknowledgment (see Official Action, page 4, para. 2, first sentence). Accordingly, new Claims 25, 26, 30 and 31 are patentable for this additional reason.

In view of the foregoing, reconsideration of all rejections and allowance of all pending claims is respectfully requested.

The Commissioner is hereby authorized to charge any fees required under 37 C.F.R. §§1.16 and 1.17 or to credit any overpayment to Deposit Account No. 16-1445.

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